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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/994,412	11/27/2001	Ulrich Certa	20787	7504

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EXAMINER	
CHONG, KIMBERLY	
ART UNIT	PAPER NUMBER
1635	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/994,412	CERTA ET AL.	
	Examiner	Art Unit	
	Kimberly Chong	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,6 and 9-12* is/are pending in the application.

4a) Of the above claim(s) *1-3 and 6* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 November 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group II, claims 9-12, in the reply filed on 11/20/2007 is acknowledged. Claims 1-3 and 6 are withdrawn as being drawn to a non-elected invention.

Status of Application/Amendment/Claims

Applicant's response filed 08/06/2007 has been considered. Rejections and/or objections not reiterated from the previous office action mailed 04/04/2007 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 9-12 are currently under examination in the application.

Oath/Declaration

The oath or declaration filed 03/22/2006 is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

> The oath or declaration is defective because:
> Non-initialed and/or non-dated alterations have been made to the oath or declaration. Specifically, alterations were made for the citizenship of inventor Ulrich Certa that were not initialed. See 37 CFR 1.52(c).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 9-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Heifetz et al. (WO 99/61631 cited on Form PTO-1449 filed 08/26/2002), Fire et al. (US Patent No. 6,506,559 cited on PTO Form 892 mailed 04/04/2007), Kreutzer et al. (WO 00/44895 cited on PTO Form 892 mailed 04/04/2007), Worsley et al. (Gynecologic Oncology 1997) and Lundstrom K. (cited on Form PTO-892 mailed 09/07/05).

The instant claims are drawn to a process for inhibiting expression of a human cyclin gene in mammalian cells or tissues comprising infecting said cells or tissue with a first set of viral particles expressing a sense RNA strand and a second set of viral particles expressing an antisense RNA strand, wherein the cells or tissue are infected with equal amounts of viral particles, wherein the sense and antisense RNA strands comprise homologous nucleotide sequences to a portion of said target gene, wherein the virus is an alphavirus, wherein the target gene is eukaryotic, viral or synthetic and the homologous nucleotide sequence is at least 50 bases in length and is specific for a target gene.

Heifetz et al. teach production of a double stranded interfering RNA comprising introducing into plant cells DNA sequences encoding a sense RNA strand and an antisense RNA strand into an expression vector wherein the sense and antisense RNA

strands are complementary to each other and form a double stranded RNA (see page 8). Heifetz et al. teach the complementary regions can be 15, 50 or 500 nucleotides in length (see page 11). Heifetz et al. teach the DNA sequences are preferably operably linked to one or more promoters wherein the promoter is a heterologous promoter (see page 10 last paragraph to the top of page 11). Heifetz et al. teach the DNA sequences that encode a sense strand or an antisense strand are in separate vectors (see pages 8-9). Heifetz et al. teach viral vectors can be used to introduce the DNA molecules into the plant cells (see page 11) and further teach methods of altering the expression of a target gene by introducing a vector comprising said DNA sequences as stated above (see pages 12-13 and Examples 1 and 3).

Fire et al. teach double stranded RNA wherein the duplex regions of the RNA are capable of hybridizing with the target gene wherein the length of the duplex regions are from 25 to 400 bases (see columns 7-8). Fire et al. teach the target gene may be derived from any cell of any organism wherein the organism may be a virus, a plant, animal or human (see column 8, lines 12-20) and teach methods of introducing the dsRNA into cells comprising contacting cells with a viral particle wherein a viral construct expresses said dsRNA (see column 9, lines 49-55).

Kreutzer et al. teach a method if inhibiting expression of a target gene in mammalian murine cells wherein the dsRNA or vector expressing said dsRNA can be enclosed in a viral particle (see page 3, lines 31-36). Kreutzer et al. teach the dsRNA has from 10 to 1000 base pairs (see page 4, lines 1-5).

Worsley et al. teach human Cyclin D1 gene is found to be overexpressed in ovarian cancers (see page 189). Worsley et al. teach Cyclin D1 regulates the activity of cyclin-dependent protein kinases and has been demonstrated to act as an oncogene in cancers such as ovarian (see page 189).

Lundstrom teach alphavirus vectors, such as Semliki Forest Virus vectors, for production of high titer viral particles comprising nucleic acid sequences for delivery to cells (see page 680).

It would have been obvious to one of skill in the art to incorporate separately an antisense RNA strand and a sense RNA strand into viral particles for delivery of a dsRNA to inhibit expression of a target gene, namely a Cyclin D 1 gene as taught by Worsley et al. It would have been obvious to one of ordinary skill in the art at the time the invention was made to use an alphavirus vector, as taught by Lundstrom, to deliver the sense and antisense RNA fragment to plant cells, as taught by Heifetz et al. because Lundstrom teach production of viral particles from alphavirus vectors allow direct non-viral transfection of cell lines that results in higher fold expression levels compared to DNA vectors.

One of skill in the art would have been motivated to use viral particles as taught by Fire et al. and Kreutzer et al. to deliver the antisense and sense strands taught by Heifetz et al. because Fire et al. teach viral particles delivering nucleic acids is an efficient way to introduce the RNA into the cells. Similarly, Kreutzer et al. teach it is advantageous to delivery dsRNA or vectors encoding dsRNA using viral particles. Heifetz et al. does not specifically teach infection of cells with equal amounts of an

antisense or sense RNA fragments or equal amounts a viral particle consisting of a RNA sense fragment or antisense RNA fragments and an alphavirus vector. Heifetz et al. teach treating plant cells with a sense RNA and an antisense RNA strand for the purposes of generating dsRNA molecules for interference of expression of a target gene and teach delivery of these sense and antisense RNA strands sequentially to cells wherein the sense and antisense strands form dsRNA, therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use equal amounts of sense and antisense RNA strands and infect cells with equal volumes of viral particles comprising sense and antisense RNA strands for the purposes of forming a dsRNA molecule. One of skill in the art would have motivated to use equal volumes of a viral particle comprising a sense RNA and a viral particle comprising an antisense RNA to allow efficient formation of dsRNA molecules for the purposes of interfering with gene expression.

Moreover because Worsley et al. teach human Cyclin D1 acts as an oncogene a plays a role in the progression of ovarian cancer in humans, one of skill in the art would have been motivated to target a human Cyclin D1 gene to provide treatment for ovarian cancer. One would have been motivated to use alphaviral particles for delivery of sense and antisense RNA strands because Lundstrom specifically teach alphaviral particles are known for their extremely broad host range and therefore capable of infecting numerous cell types (see page 680 and Table 1). Lundstrom teach RNA molecules are in vitro transcribed from the plasmid vectors (see Figure 1) and alphaviral vectors are

easy to produce and have the ability to produce high titer viral particles that make them favorable for gene therapy applications (see page 680).

One of skill would have had a reasonable expectation of success given that Heifetz et al. teach efficient expression of a sense and antisense vector from different constructs and Fire et al. and Kreutzer et al. teach the use of viral particles to delivery RNA is an efficient method of delivery to cells. Further, one would have a reasonable expectation of success at using an alphavirus vector for delivery because Lundstrom teach generation of alphavirus vectors, efficient production of high titer alphavirus particles and use in gene transfer into cells. Further Lundstrom teach an efficient high titer alphavirus viral particle packaging system.

Thus in the absence of evidence to the contrary, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Although the foregoing represents a new rejection necessitated by the filing of new claims, Applicant's argument filed 08/06/2007 will be responded to as they apply to the some of the references used in the new rejection above.

Applicant argues that while Heifetz et al. suggests that sense and antisense strands may be introduced together or separately, Heifetz et al. does not teach or suggest that the use of one method over the other would produce superior results, namely using separate viral particles to introduce a sense and an antisense strand.

Applicant points to support for the superiority of introducing separate viral particles comprising a sense and an antisense strand in Examples 6 and 7 of the specification.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., superior results using separate viral particles comprising a sense and an antisense strand) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Moreover, Examples 6 and 7 appear to represent a single experiment, without any data shown, to which Applicant draws the conclusion of "superior results" when using separate sense and antisense strands in viral particles.

Thus, Applicant' arguments are not persuasive.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly Chong whose telephone number is 571-272-3111. The examiner can normally be reached Monday thru Friday between 7-4 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Schultz can be reached at 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now

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/Kimberly Chong/
Examiner
Art Unit 1635